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EXAMINER

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UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

Ex parte MITCHELL SHIRVAN, ELLAT SHINAR,
ORIL FRENKEL, ADI ZULOFF-SHANI, MARINA BUBIS,
EILAT BAIN, and IRENE GILLIS

Appeal 2016-002106¹
Application 13/669,134
Technology Center 1600

Before FRANCISCO C. PRATS, RYAN H. FLAX, and
RACHEL H. TOWNSEND, *Administrative Patent Judges*.

PRATS, *Administrative Patent Judge*.

DECISION ON APPEAL

This appeal under 35 U.S.C. § 134(a) involves claims to compositions containing activated leukocytes. The Examiner rejected the claims as being directed to subject matter ineligible for patenting.

We have jurisdiction under 35 U.S.C. § 6(b). We affirm.

STATEMENT OF THE CASE

Appellants' invention is "directed to a method for making an activated leukocyte composition (ALC) derived from blood (*e.g.*, obtainable or obtained from a whole blood sample)." Spec. ¶ 8. The activated leukocyte

¹ Appellants state that "MacroCure Ltd. is the real party in interest." App. Br. 1.

composition is prepared by performing three steps: (1) incubating leukocytes at room temperature for about 8 to 20 hours, or at elevated temperatures for about 30 minutes to 12 hours (Spec. ¶ 45), (2) subjecting the incubated leukocytes to hypo-osmotic shock by contacting them with distilled water for about 25–45 seconds (*id.* ¶ 46), and (3) restoring the osmotically shocked leukocytes to isotonicity in a sodium chloride solution (*id.*). In a preferred embodiment, the activated leukocytes are subsequently incubated with coagulated plasma. *Id.* ¶ 48.

The Specification discloses that a suitable leukocyte-containing starting material may be a fresh buffy coat (“FBC”), which is obtained by centrifuging a blood sample. *See id.* ¶ 39; *see also id.* ¶ 76 (Example 1).

The Specification discloses:

For purposes of the present invention, leukocyte activation is defined as a process involving at least one stage, by which the cells (leukocytes) undergo a transition from a quiescent to a functionally active state which is accompanied by synthesis of biologically active substances or translocation of pre-synthesized substances, e.g., cytokines including IL-8, from the cytoplasm to the cellular membrane or their release into extracellular medium (which in this case is serum). Activation of leukocytes *in vivo* may involve migration of the cells closer to and along the blood vessel wall, which is mediated by P-selectin (and increased CD42b expression), increased adhesion of leukocytes to the endothelial wall, spreading and extravasation, which is mediated to a large degree by activated CD11b that interacts with endothelial ligands ICAM-1 and ICAM-2; migration to the focus of inflammation via interaction with extracellular matrix proteins e.g., laminin) and functional responses to inflammatory stimuli such as respiratory burst, degranulation, phagocytosis and release of cytokines.

Id. ¶ 44.

The Specification discloses that “activation of the leukocytes, at least as a result of the first incubation, may be indicated by increased expression of activated form of CD11b receptor on leukocyte populations including granulocytes, monocytes and lymphocytes, and higher expression levels of CD69, a lymphocyte-specific activation marker.” Spec. ¶ 44. The Specification discloses that altered expression levels of those marker molecules, “is assessed from the standpoint of the leukocytes contained in a ‘fresh buffy coat’ (as described herein), without being subjected to an incubation.” *Id.*

The Specification discloses that the activated leukocyte compositions can be applied directly to wounds to aid in healing, or can be combined with a dressing such as gauze or a bandage to be applied to the wound, or combined with a scaffold, such as a gel, which may be implanted in a patient. *Id.* ¶¶ 22–24.

The Specification states that the “disclosed invention is also believed to include an unexpectedly and relatively high percentage of activated monocytes (compared to blood) and a relatively higher percentage of CD8 T-cells compared to CD4 T-cells.” *Id.* ¶ 28.

Claims 21 and 28, the independent claims on appeal, are representative, and read as follows (App. Br. 16–17):

21. A composition comprising activated leukocytes, wherein the composition comprises:
 - a) about 40% to about 90% granulocytes;
 - b) about 5% to about 20% monocytes; and
 - c) about 5% to about 30% lymphocytes.
28. An article of manufacture comprising:
 - a composition comprising activated leukocytes, wherein the composition comprises:

- a) about 40% to about 90% granulocytes;
- b) about 5% to about 20% monocytes; and
- c) about 5% to about 30% lymphocytes; and
a dressing.

The sole rejection before us for review is the Examiner's rejection of claims 21–35, 45, and 46, under 35 U.S.C. § 101, as being directed to subject matter ineligible for patenting. Final Action 2–3 (entered October 31, 2014).

DISCUSSION

The Examiner's Position

In rejecting claims 21–35, 45, and 46 as being directed to subject matter ineligible for patenting, the Examiner found that the composition recited in the rejected claims “is not markedly different in structure from [a] naturally occurring [composition].” Final Action 2. In particular, the Examiner reasoned:

The claimed percentage of each subtype of leukocyte, i.e. about 40-to about 90 % of granulocytes, about 5 to about 20% of monocytes and about 5 to 30% lymphocytes, neutrophil about 52-78% etc is not markedly different from natural occurring in human blood, i.e. neutrophil about 62 - 70 %; eosinophil- about 2-4 %; basophil- about 0.4 -1 %; lymphocyte - about 30-35 %; monocytes - about 5-7 %.

Id.

The Examiner reasoned, moreover, that “[a]dding a dressing to a composition [is] routine and conventional and well –understood” and that “[a]dding a material suitable for implantation is nothing more than just a field of use.” *Id.* at 3.

Analysis

As stated in *In re Oetiker*, 977 F.2d 1443, 1445 (Fed. Cir. 1992):

[T]he examiner bears the initial burden . . . of presenting a *prima facie* case of unpatentability. . . .

After evidence or argument is submitted by the applicant in response, patentability is determined on the totality of the record, by a preponderance of evidence with due consideration to persuasiveness of argument.

Appellants do not persuade us that a preponderance of the evidence fails to support the Examiner’s conclusion that the rejected claims recite subject matter ineligible for patenting under 35 U.S.C. § 101.

35 U.S.C. § 101 states that “[w]hoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.”

The Supreme Court has “long held that this provision contains an important implicit exception: Laws of nature, natural phenomena, and abstract ideas are not patentable.” *Alice Corp. Pty. Ltd. v. CLS Bank Intern.*, 134 S. Ct. 2347, 2354 (2014).

As to natural phenomena, the Supreme Court has held ineligible for patenting claims directed to a combination strains of naturally occurring nitrogen-fixing bacteria, and claims directed to unmodified DNA isolated from a human. *See Funk Brothers Seed Co. v. Kalo Inoculant Co.*, 333 U.S. 127 (1948) (nitrogen-fixing bacteria); *Association for Molecular Pathology v. Myriad Genetics, Inc.*, 133 S. Ct. 2107 (2013) (isolated DNA).

Our reviewing court has summarized the Supreme Court’s two-part test for distinguishing between claims to patent-ineligible exceptions, and claims to patent-eligible applications of those exceptions, as follows:

Step one asks whether the claim is “directed to one of [the] patent-ineligible concepts.” [*Alice*, 134 S. Ct. at 2354]. If the answer is no, the inquiry is over: the claim falls within the ambit of § 101. If the answer is yes, the inquiry moves to step two, which asks whether, considered both individually and as an ordered combination, “the additional elements ‘transform the nature of the claim’ into a patent-eligible application.” *Id.* (quoting *Mayo* [*Collaborative Services v. Prometheus Labs, Inc.*, 132 S. Ct. 1289, 1297 (2012)]).

Step two is described “as a search for an ‘inventive concept.’” *Id.* (quoting *Mayo*, 132 S. Ct. at 1294). At step two, more is required than “well-understood, routine, conventional activity already engaged in by the scientific community,” which fails to transform the claim into “significantly more than a patent upon the” ineligible concept itself. *Mayo*, 132 S. Ct. at 1298, 1294.

Rapid Litigation Mgmt. Ltd. v. CellzDirect, Inc., 827 F.3d 1042, 1047 (Fed. Cir. 2016) (paragraphing added).

In the present case, claim 21 recites “[a] composition comprising activated leukocytes.” App. Br. 16. Claim 21 recites that “the composition comprises: a) about 40% to about 90% granulocytes; b) about 5% to about 20% monocytes; and c) about 5% to about 30% lymphocytes.” *Id.*

The Examiner found, and Appellants do not dispute, that human blood contains about 62–70 % neutrophils, about 2–4 % eosinophils, and about 0.4–1 % basophils, and together these cell types constitute the granulocytes in blood. Final Action 2; *see also* Spec. ¶ 2 (granulocytes are composed of neutrophils, eosinophils, and basophils). The Examiner also found that human blood contains about 5–7 % monocytes and about 30–35 %

lymphocytes. Final Action 2. Thus, as is evident, and is undisputed on this record, the composition recited in claim 21 contains granulocytes, monocytes, and lymphocytes in percentages in which those cells appear in human blood.

Moreover, as the Examiner found, and is confirmed by Appellants' Specification, human blood contains activated leukocytes. *See* Ans. 4; *see also* Spec. ¶ 28 (disclosing that the inventive composition has unexpectedly higher percentage of activated monocytes “compared to blood”); Spec. ¶ 44 (explaining characteristics of “[a]ctivation of leukocytes *in vivo*”).

Thus, because human blood contains each of the cell types required by claim 21, in the amounts required by the claim, as well as including “activated leukocytes,” we agree with the Examiner that claim 21 is directed to a natural product, and therefore is not eligible for patenting under § 101 under the *Mayo* framework. Appellants' arguments do not persuade us to the contrary.

Appellants contend that claim 21 is eligible for patenting under § 101 because the claim does not tie up all activated leukocyte compositions, as evidenced by the differences between the claimed composition and prior art activated leukocyte compositions. App. Br. 6–7.

Our reviewing court has expressly rejected similar contentions regarding preemption, however, stating that a patentee's “attempt to limit the breadth of the claims by showing alternative uses . . . outside of the scope of the claims does not change the conclusion that the claims are directed to patent ineligible subject matter.” *Ariosa Diagnostics, Inc. v. Sequenom, Inc.*, 788 F.3d 1371, 1379 (Fed. Cir. 2015). The court explained that, “[w]hile preemption may signal patent ineligible subject matter, the absence of

complete preemption does not demonstrate patent eligibility. . . . Where a patent’s claims are deemed only to disclose patent ineligible subject matter under the *Mayo* framework . . . preemption concerns are fully addressed and made moot.” *Id.*

Appellants contend that the composition recited in claim 21 does not encompass a natural product because leukocytes require activation, by the methods taught in the Specification for example, whereas whole blood is a source material that contains unactivated quiescent leukocytes. App. Br. 7–8, (citing Spec. ¶¶ 36–37); *see also id.* at 10–12 (contending that the claimed composition has markedly different characteristics than blood); *see also* Reply Br. 1–2 (contending that no natural product exists in which all three types of leukocytes are activated in the claimed percentages).

For the reasons discussed above, however, Appellants do not persuade us that claim 21 fails to encompass human blood. In particular, as discussed above, human blood contains activated leukocytes as well as the cell types required by claim 21 in the claimed percentages. Contrary to Appellants’ argument, moreover, claim 21 does not require the claimed composition to contain any particular amount of activated leukocytes, but instead recites only that the claimed composition “compris[es] activated leukocytes.” App. Br. 16.

Claim 21, in addition, does not require any of the granulocytes, monocytes, or lymphocytes to be activated, but instead simply recites that “the composition comprises: a) about 40% to about 90% granulocytes; b) about 5% to about 20% monocytes; and c) about 5% to about 30% lymphocytes.” *Id.* As is evident, claim 21 says nothing about whether the

granulocytes, monocytes, or lymphocytes are activated, contrary to Appellants' argument.

We acknowledge the disclosure in Appellants' Specification, discussed above, that incubation, osmotic shock, and restoration of isotonicity of a fresh buffy coat preparation yields a composition with a substantial percentage of activated leukocytes. As noted above, however, the current language in claim 21 is sufficiently broad to encompass human blood. To the extent Appellants seek to limit the interpretation of claim 21 to their preferred disclosed embodiments, it is well settled that "while 'the specification [should be used] to interpret the meaning of a claim,' courts must not 'import[] limitations from the specification into the claim.' . . . [I]t is improper to 'confine the claims to th[e] embodiments' found in the specification" *In re Trans Texas Holdings Corp.*, 498 F.3d 1290, 1299 (Fed. Cir. 2007) (quoting *Phillips v. AWH Corp.*, 415 F.3d 1303, 1323 (Fed. Cir. 2005), citations omitted, bracketed text in internal quotes in original); *see also In re Bigio*, 381 F.3d 1320, 1325 (Fed Cir. 2004) ("[A]bsent claim language carrying a narrow meaning, the PTO should only limit the claim based on the specification . . . when [it] expressly disclaims the broader definition.").

In sum, for the reasons discussed, Appellants do not persuade us that a preponderance of the evidence fails to support the Examiner's conclusion that claim 21 recites subject matter ineligible for patenting under 35 U.S.C. § 101. We, therefore, affirm the Examiner's rejection of claim 21. Because they were not argued separately, claims 22–27, 45, and 46 fall with claim 21. *See* 37 C.F.R. § 41(c)(1)(iv).

Claim 33 recites “[t]he composition of claim 21, further comprising as a matrix or scaffold a material suitable for implantation in a person.” App. Br. 18. Appellants contend that, in addition to arguments discussed above, “the recitations of ‘a matrix or scaffold’ add further elements that do not ‘tie-up’ other activated leukocyte compositions.” *Id.* at 8. Appellants also contend that claim 33’s “recitation of ‘a matrix or scaffold’ add[s] further elements that represent additional marked differences to any naturally occurring product.” *Id.* at 13.

As discussed above, the composition recited in claim 21 encompasses human blood. Although we note that claim 33 requires the additional presence of a matrix or scaffold in that composition, Appellants do not explain, specifically, *how* combining a matrix or scaffold with blood would yield a composition with properties significantly different from a blood composition included in any conventional packaging medium used for implantable therapeutic compositions. At step two of the *Mayo* framework, more is required than “well-understood, routine, conventional activity already engaged in by the scientific community,” in order to transform the claim into “significantly more than a patent upon the” ineligible concept itself. *Mayo*, 132 S. Ct. at 1298, 1294. While Appellants urge that combining the composition of claim 21 with the matrix or scaffold recited in claim 33 results in a composition markedly different from a naturally occurring product, Appellants do not explain, specifically, what those alleged differences are, or why those differences demonstrate patent eligibility, under the *Mayo* framework.

As discussed above, moreover, that the composition of claim 33 might not preempt every application of activated leukocytes does not demonstrate

that the composition is eligible for patenting under § 101. *See Ariosa Diagnostics v. Sequenom*, 788 F.3d at 1379 (“While preemption may signal patent ineligible subject matter, the absence of complete preemption does not demonstrate patent eligibility. . . . Where a patent’s claims are deemed only to disclose patent ineligible subject matter under the *Mayo* framework . . . preemption concerns are fully addressed and made moot.”).

In sum, for the reasons discussed, Appellants do not persuade us that a preponderance of the evidence fails to support the Examiner’s conclusion that claim 33 recites subject matter ineligible for patenting under 35 U.S.C. § 101. We, therefore, affirm the Examiner’s rejection of claim 33, and its dependent claims 34 and 35, which were not argued separately.

Claim 28, reproduced above, recites in independent form “[a]n article of manufacture” composed of “a dressing” and the composition recited in claim 21. App. Br. 17. Appellants contend that each of the recitations of “an article of manufacture” and “a dressing” is “a further element that does not ‘tie-up’ other activated leukocyte compositions.” App. Br. 8. Moreover, Appellants contend, “the recitation of ‘a dressing’ adds a further element that represents additional marked differences to any naturally occurring product.” *Id.* at 13.

For reasons similar to those discussed above as to claim 33, we do not find these arguments persuasive. As discussed above, the composition recited in claim 21 encompasses human blood. We note that claim 28 requires claim 21’s composition to be present in an article of manufacture that also contains a dressing. Claim 28, however, does not require the cell-containing composition (i.e., blood) to be combined with or associated with the dressing in any particular manner, such that the dressing might modify

the properties of the blood, or, as an ordered combination, result in a product having properties significantly different from an article composed simply of blood and a container.

Appellants, moreover, do not explain specifically *how* including blood in an article of manufacture containing a dressing, in the manner required by claim 28, would modify the blood to have significantly different properties. That is, while Appellants urge that combining the composition of claim 21 with the dressing recited in claim 28 results in a composition markedly different from a naturally occurring product, Appellants do not explain, specifically, with reference to the actual limitations required by the claim, what those alleged differences are, or why those differences demonstrate patent eligibility, under the *Mayo* framework.

As discussed above, moreover, that the composition of claim 28 might not preempt every application of activated leukocytes does not demonstrate that the composition is eligible for patenting under § 101. *See Ariosa Diagnostics v. Sequenom*, 788 F.3d at 1379.

In sum, for the reasons discussed, Appellants do not persuade us that a preponderance of the evidence fails to support the Examiner's conclusion that claim 28 recites subject matter ineligible for patenting under 35 U.S.C. § 101. We, therefore, affirm the Examiner's rejection of claim 28, as well as its dependent claims, which were not argued separately.

SUMMARY

For the reasons discussed, we affirm the Examiner's rejection of claims 21–35, 45, and 46, under 35 U.S.C. § 101, as being directed to subject matter ineligible for patenting.

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TIME PERIOD

No time period for taking any subsequent action in connection with this appeal may be extended under 37 C.F.R. § 1.136(a).

AFFIRMED